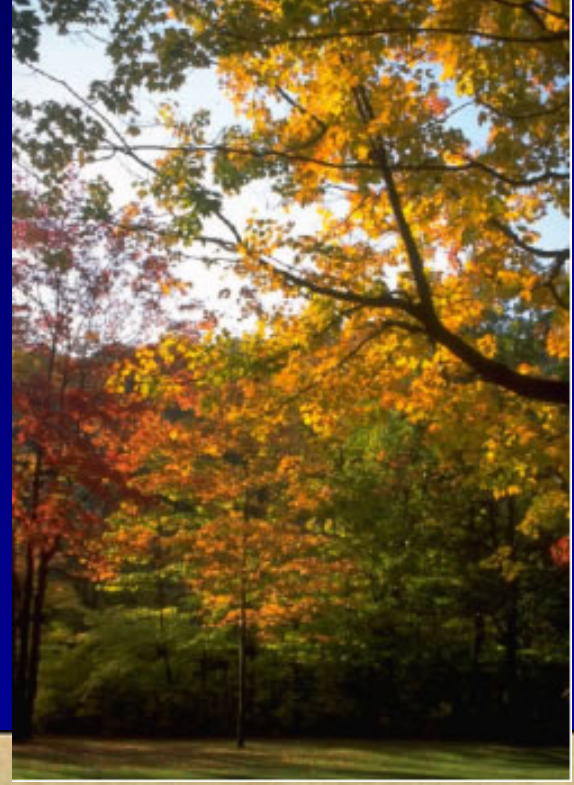
Tick-Associated Illness

COL Matthew Dolan
Defense Institute for Medical Operations (DIMO)
Brooks City-Base, TX



Ixodes scapularis (dammini)

Life Cycle

Larva → Mice (infected)

Blood meal

Nymph → Humans

Blood meal

Adult → Deer (not infected)

Blood meal

Impregnated female (lays 20,000 eggs)


1
2

Lime Disease

Limes Disease

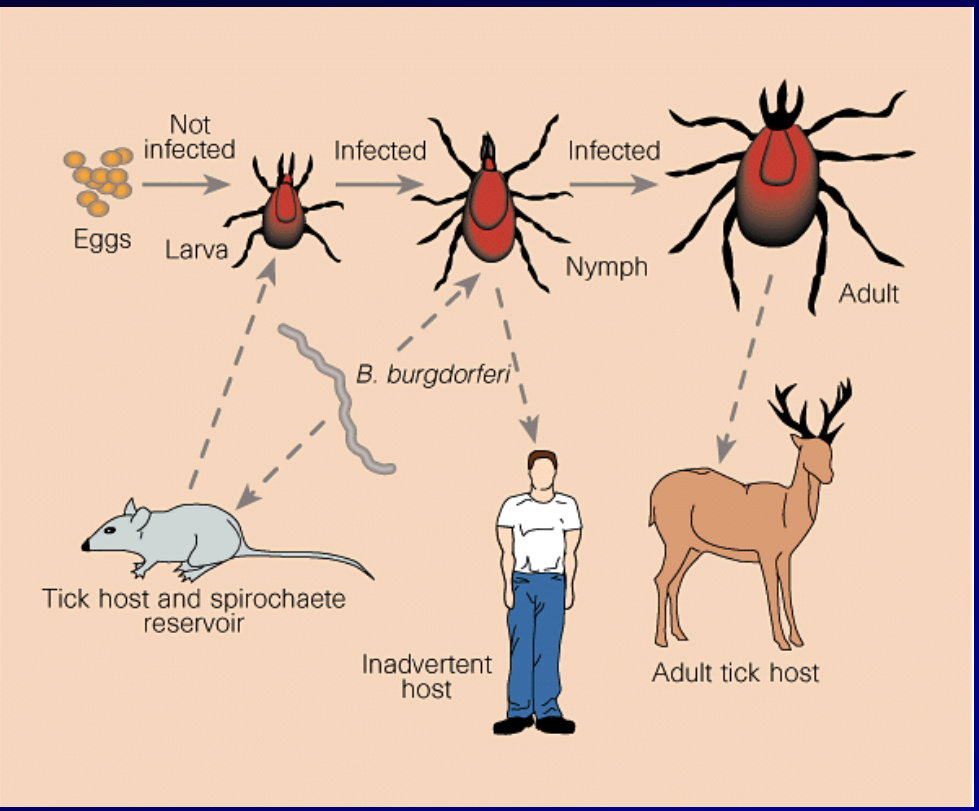
Lyme Disease

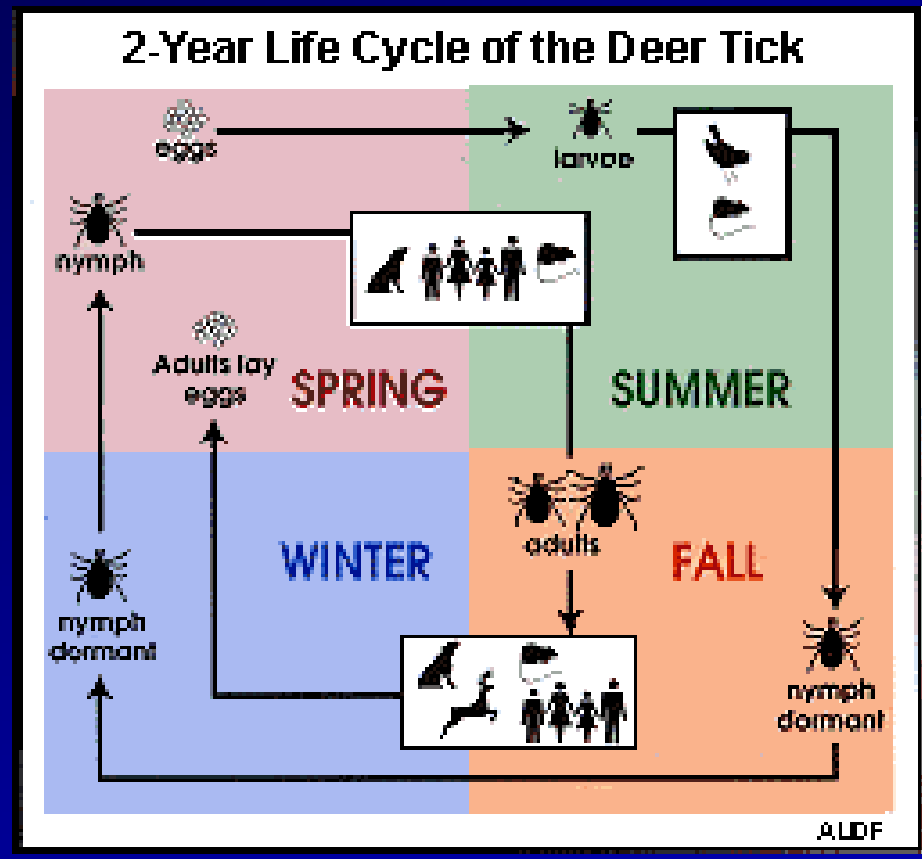
Lyme Disease- History

- 1975 Outbreak in children in Lyme, CT
  - Thought to be juvenile rheumatoid arthritis
- Previously recognized in Europe
  - Erythema chronicum migrans (ECM)
  - Bannwarth syndrome
  - Acrodermatitis chronica atrophicans

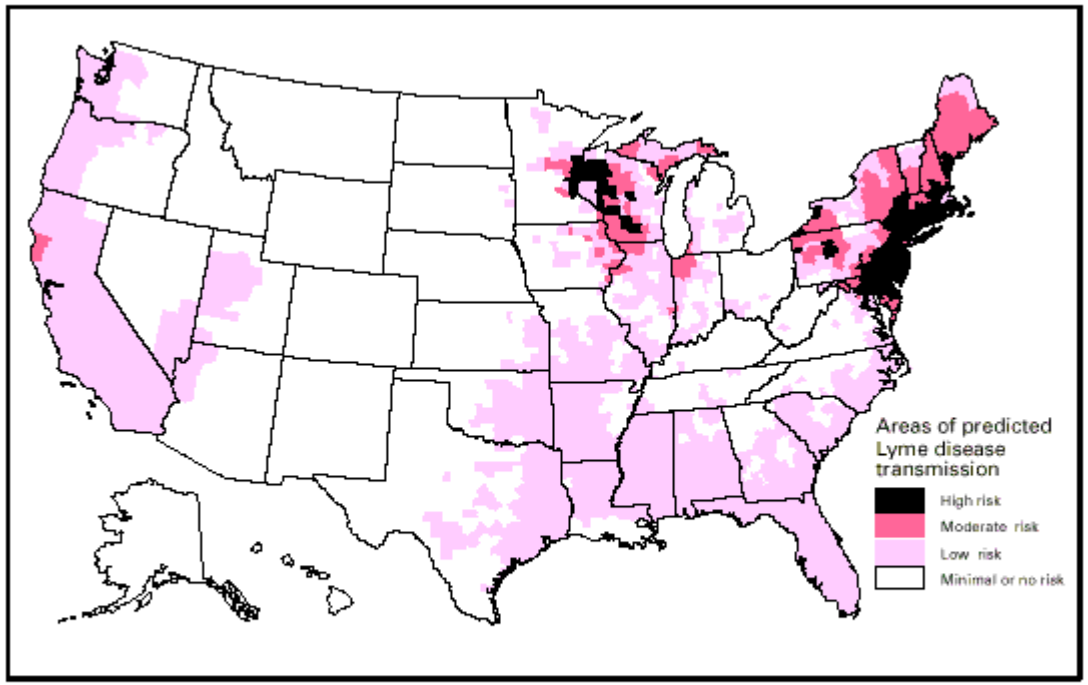
Lyme Disease

- Range North America, Europe, Asia
- Most common vector born illness in US
- Ixodes species
  - NE-Midwest: I scapularis (dammini)
  - West: I. pacificus
  - Europe: I ricinus
  - Asia: I. persulatus
- Questing
  - Adult: spring, fall
  - Nymph May-July
  - Larvae: Aug, SEP.


Not infected
Infected
Infected
Eggs
Larva
Nymph
Adult
B. burgdorferi
Tick host and spirochaete reservoir
Inadvertent host
Adult tick host

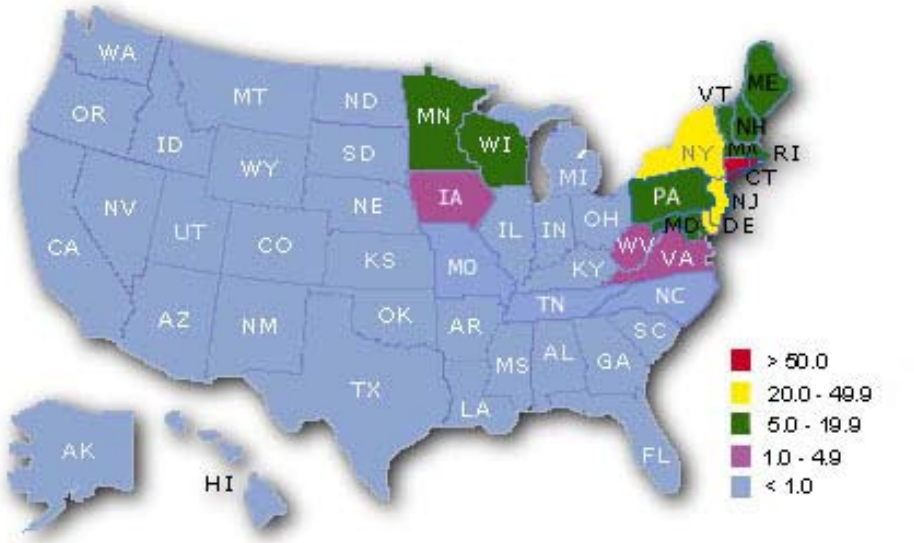

2-Year Life Cycle of the Deer Tick
eggs
larvae
nymph
Adults lay eggs
SPRING
SUMMER
WINTER
adults
FALL
nymph dormant
nymph dormant
ALDF

National Lyme disease risk map with four categories of risk



Note: This map demonstrates an approximate distribution of predicted Lyme disease risk in the United States. The true relative risk in any given county compared with other counties might differ from that shown here and might change from year to year. Risk categories are defined in the accompanying text. Information on risk distribution within states and counties is best obtained from state and local public health authorities.

Lyme Disease, 2000



Case numbers

Incidence/100,000

American Lyme Disease Foundation

Lyme- Epidemiology

- Median age 28 years
- M:F 1:1
- Bimodal
- Children, middle aged adults
- US- 1 may- 30 OCT (JUN-JUL peak)
- Dogs, horses, cattle also infected

Lyme Disease

- Stage 1: localized infection
- Stage 2: disseminated infection
- Stage 3: persistent infection

Lyme disease
Stage 1

- Erythema migrans (EM) at tick bite site
- Thigh, groin, axilla common
- Median diameter 15 cm
- Head- linear streak from hairline
- Hot, not painful
- 25% atypical presentation
- CT-314 Lyme patients
  - 31% recalled tick bite at site
  - Lesions 3-32d after tick bite

Steere, Ann Int Med, 1983, 99:76

Erythema Migrans

- Myalgia, fatigue
- Headache, meningeal irritation, encephalopathy
- Fever, chills, migratory musculoskeletal pain
- Hepatitis, splenomegally
- Sore throat
- Non productive cough
- Testicular swelling

Erythema migrans

Lyme Disease
Stage 2

- Multiple annular lesions
- Days to weeks after infection
- Fade in 3-4 weeks
- Skin, nervous system, heart, joint symptoms occur in weeks to months

Lyme Disease
Stage 2- Neuro

- 15% of cases
- Meningitis
- Encephalitis
- Cranial neuritis
- Motor/sensory radiculoneuritis
- Mononeuritis multiplex
- Myelitis
- CSF
  - ~100 cells/mcl
  - Lymph pleocytosis
  - Intrathecal antibody

Lyme Disease
Stage 2- Cardiac

- 5% of cases
- Fluctuating AVB
- 1° AVB, Wenkebach, 3° AVB
- Myopericarditis
- Gallium scan, EKG changes
- Mild LV dysfunction
- Duration 3 d.-6 wks. (3° AVB 1 week)
- Permanent pacer not needed

Lyme Disease
Stage 2- Ocular

- Conjunctivitis
- Iritis
- Choroiditis
- Retinal hemorrhage
- Pan opthalmitis
- (keratitis stage 3)

Lyme Disease
Stage 2- Musculoskeletal Pain

- Migratory (hours –days), single location
- No swelling
- Joints, bursa, tendons
- Muscle, bone

Lyme Disease
Stage 3- Joints

- Months-years
- Joint swelling, pain
- Large joints (knee), 1-2 at a time
- More swollen than painful
- Usually hot, but not red
- Progress to remission over weeks-months
- Joint fluid 500-110,000 cells/mcl, PMN's
- HLA-DRB1*0401

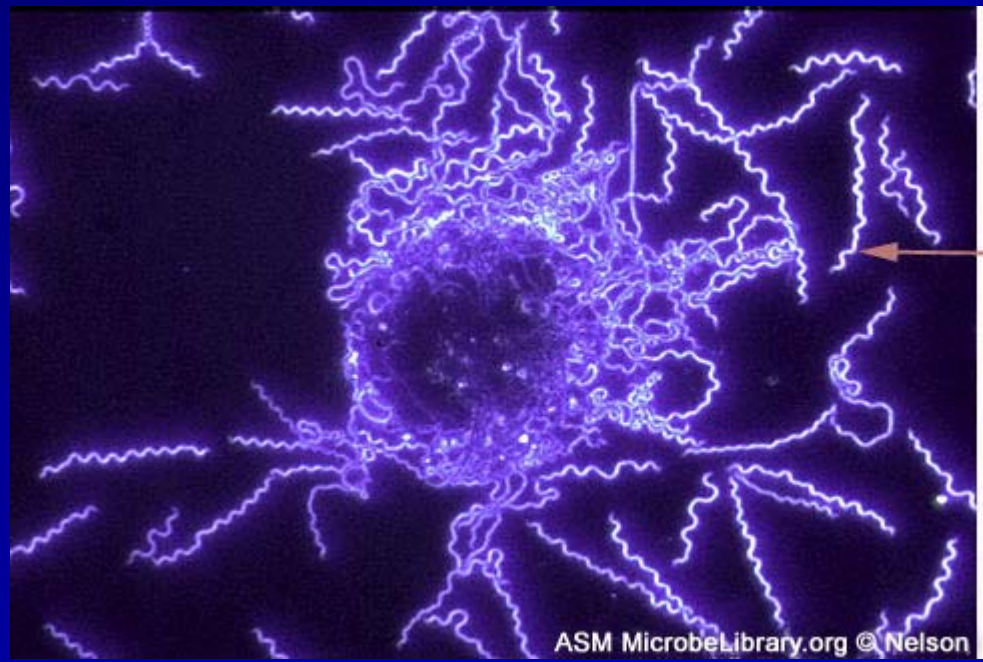
Lyme Disease
Stage 3- Neuro

- Months-years
- Sub acute encephalopathy
- Memory, mood sleep, language disturbance
- Distal paresthesias, spinal/radicular pain
- CSF protein
- SPECT changes

Lyme-Diagnostic Testing

- Elisa, Western blot
- CSF/serum antibody ratio
- PCR (synovial fluid 85% sensitive)
- ↑ESR, ↑ IgM, ↑ SGOT
- C3, C4 normal to increased

CDC


Spirochete bacteria,
Borrelia burgdorferi
ASM MicrobeLibrary.org © Nelson

Lyme- Serodiagnosis

- EM- 30-40% positive serology
- 60-70% positive 2-4 weeks later
- After 4-6 weeks 90% positive IgG
- Titer falls slowly with therapy
- 10-20% asymptomatic

Lyme Disease West Coast

Lizard

Dusty footed wood rat

Ixodes pacificus
Larvae, nymph

Ixodes neotamae
Maintains Borrelial infection
in wood rats

human

Southern Tick Associated Rash Illness (STARI)

- Ambyloma americanum
- *Borrelia lonestari*

Lyme- Coinfection

- Block Island-206 patients- 23 (11%) coinfected with Babesia
- NY- 5.5% nymphal Ixodes infected with HE
- Europe- Tick born encephalitis coinfection

Krause, JAMA 1996, 275:1657
Schwartz, NEJM, 1997, 337: 49

Lyme Disease
Oral Treatment Regimens

Drug	Dose (adult)	Dose (child)
Preferred Oral		
Amoxicillin	500 mg tid	50 mg/kg/d into 3 doses
Doxycycline	100 mg bid	Age>8y 1-2 mg/kg bid
Alternative oral		
Cefuroxime axetil	500 mg bid	30mg/kg/d into 2 doses

IDSA Guidelines CID 2000, 31(suppl): S1-14

Lyme Disease
Parenteral Treatment Regimens

Drug	Dose (adult)	Dose (child)
Preferred parenteral		
Ceftriaxone	2g iv qd	75-100 mg/kg iv qd
Alternative parenteral		
Cefotaxime	2g iv tid	150-200 mg/kg/d into 3-4 doses
Penicillin G	18-24 mil units iv/d divided into doses q4h	200,000-400,000 units/kg/d into q4h doses

IDSA Guidelines CID 2000, 31(suppl): S1-14

Lyme Disease
Treatment Indications

Indication	Treatment	Duration (d.)
Tick bite	Observe	
Erythema migrans	Oral	14-21
Acute neurological disease		
Meningitis or Radiculopathy	Parenteral	14-28
Cranial nerve palsy	Oral	14-21

IDSA Guidelines CID 2000, 31(suppl): S1-14

Lyme Disease
Treatment Indications

Indication	Treatment	Duration (d.)
Cardiac Disease		
1st or 2nd degree AVB	Oral	14-21
3rd degree AVB	Parenteral	14-21

IDSA Guidelines CID 2000, 31(suppl): S1-14

Lyme Disease: Treatment Indications

Indication	Treatment	Duration (d.)
Late disease		
Arthritis (w/o neurological disease)	Oral	28
Recurrent arthritis (after oral)	Oral or parenteral	28
Persistent arthritis (after 2 courses abx.)	Symptomatic	
CNS or peripheral nervous system disease	Parenteral	14-28
Chronic/post Lyme disease	Symptomatic	14-28

IDSA Guidelines CID 2000, 31(suppl): S1-14

Babesiosis-history

- Pharaoh Ramses II, Exodus 9:3
  - "murrain" of cattle"
- 1888 V. Babes, Romanian febrile hemoglobinuria of cattle
- 1893 Theobald Smith, F. L. Kilbourne "Texas Cattle Fever"

Babesia species

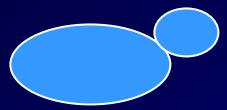
- B. microti (US)
- B. divergens (Europe)
- WA-1 (Washington state)
- MO-1 (Missouri)
- Over 100 species known

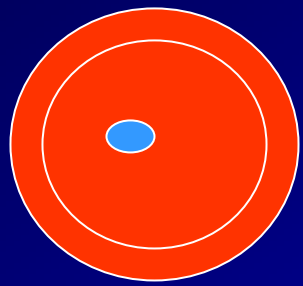
Babesia-Hosts

- B. microti
  - Small mammals, primates, humans
- B. divergens
  - rats, gerbils, cattle, humans

Babesia- Life Cycle

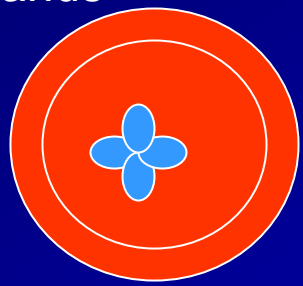
Infection of intestinal epithelium



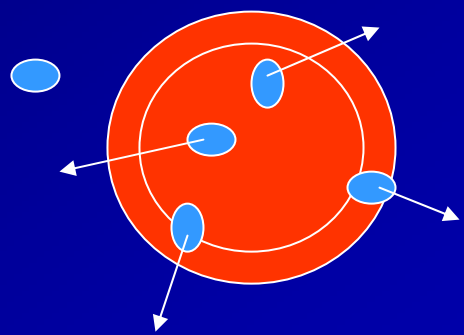


Trophozoite in RBC

Sporozoites multiply in salivary glands

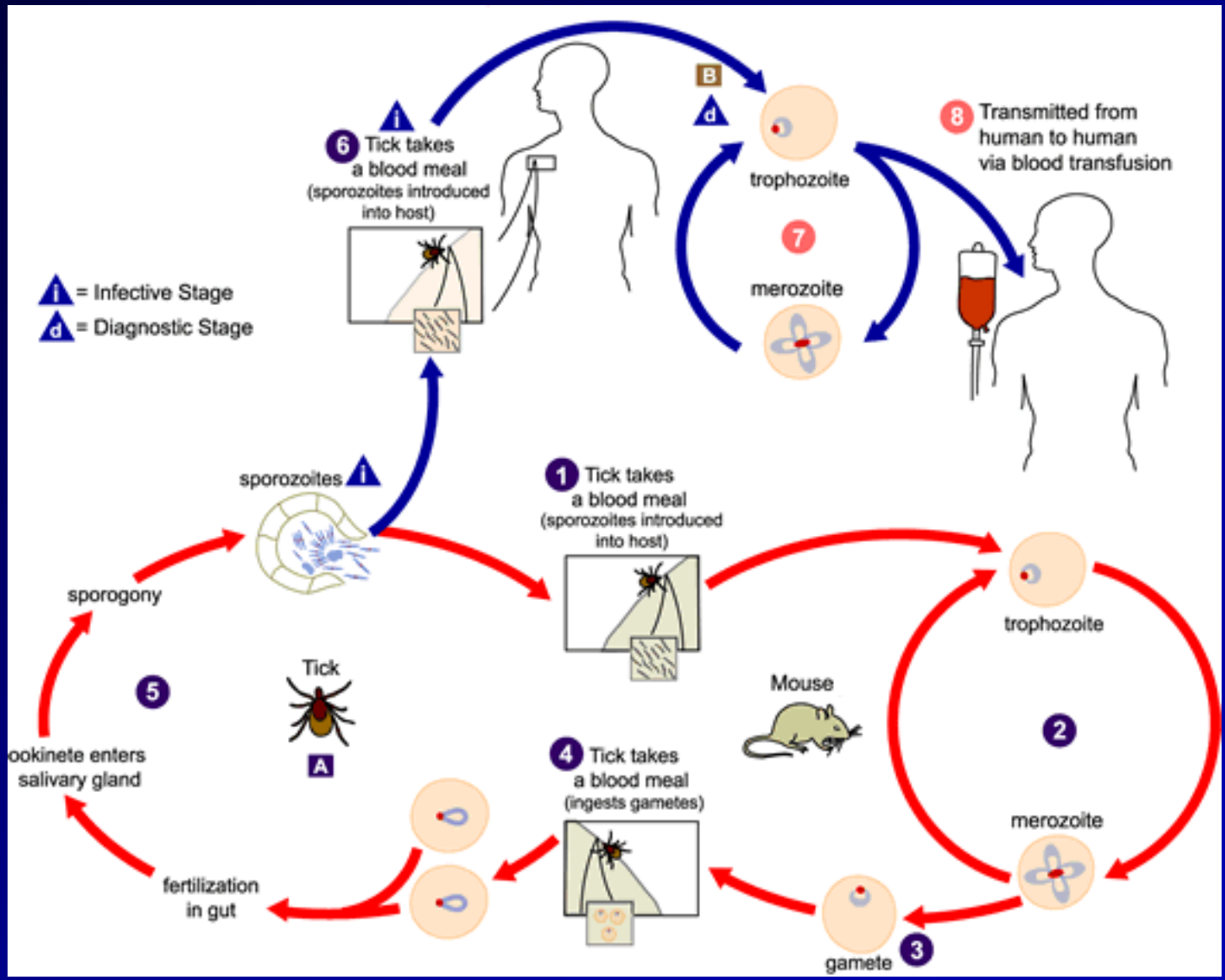


Tetrad of Merozoites



Schizonts
Asynchronous burst

Babesiosis - Life Cycle

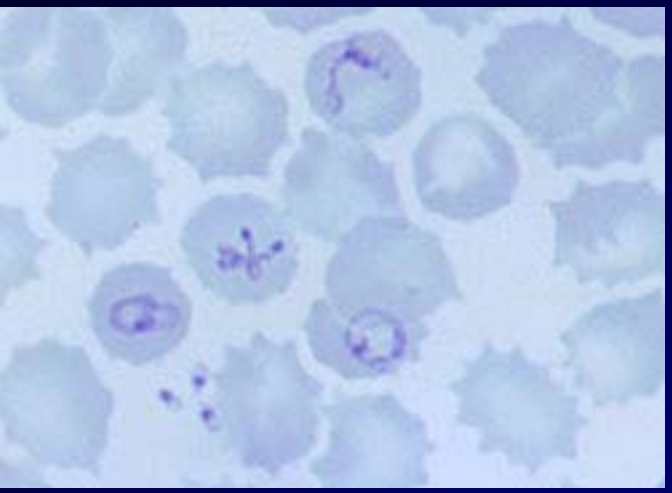


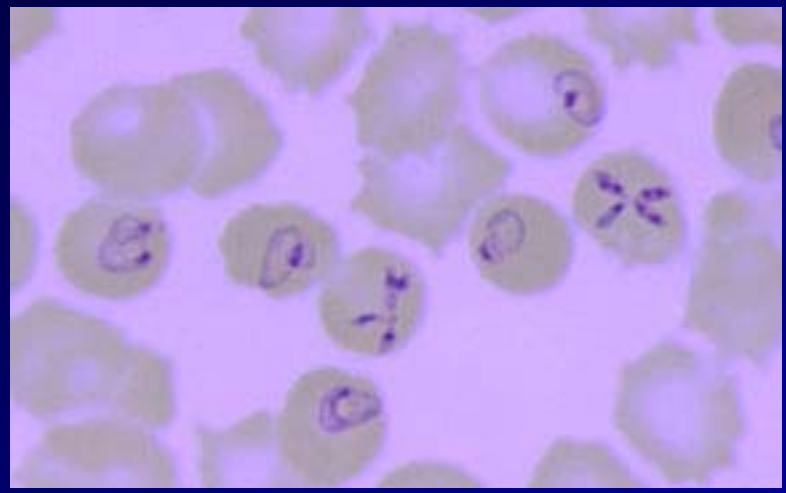
Babesiosis

- Incubation 1-3 weeks
- Symptoms
  - Gradual fever, fatigue, headache, myalgia, conjuctival injection, emotional lability
- Signs
  - Hepatomegaly, splenomegaly, jaundice
  - Rash uncommon

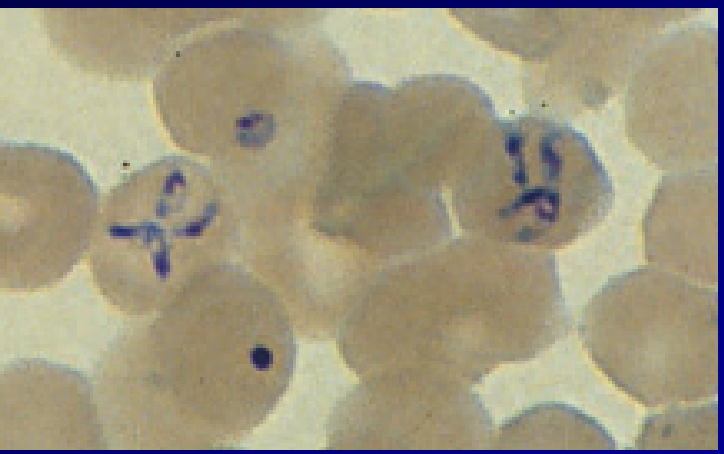
Babesia- Diagnosis

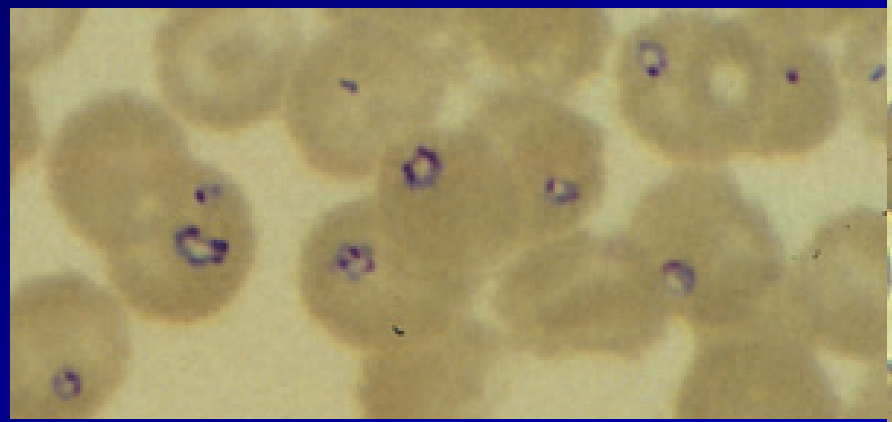
- Blood smear
- PCR
- Serology

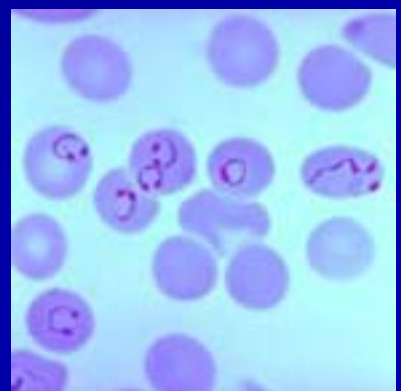




Babesia







P. falciparum

Babesiosis vs Malaria

- No pigment granules in RBC
- Extraerythrocytic parasites
- Tetrad of Merozoites forming Maltese cross

Babesiosis-Labs

- Anemia, thrombocytopenia, mild leucopenia, atypical lymphs
- ↑ ESR
- ↑ Alkaline phos., transaminases
- ↓ Complement
- Intravascular hemolysis
- UA-proteinuria, hemoglobinuria

Babesiosis- Treatment

- Supportive care
- Antimicrobial RX
- Quinine 650 mg q8h plus Clindamycin 1200mg iv q12h
- Atovaquone 750 mg bid plus azithromycin 500 mg d1, 250 mg d2-6
- Exchange transfusion

Babesia - Antimicrobial Rx

Regimen	Efficacy (%)	Toxicity (%)
Atovaquone/ azithromycin	65	15
Quinine/ clindamycin	73	72

Krause, NEJM, 2000, 343:1454

Babesiosis - Serious Disease

- Age>40
- Asplenic
- Decreased cell-mediated immunity
  - HIV
  - Steroids

Babesiosis- Fatality

- B. microti 5-6% hospitalized cases
- B. divergens 40%

Coinfection

- RI/CT serosurvey 1156 subjects
- 14% Lyme + also Babesia +
- 23% Babesia + also Lyme +
- Symptoms more frequent, longer duration than Lyme alone

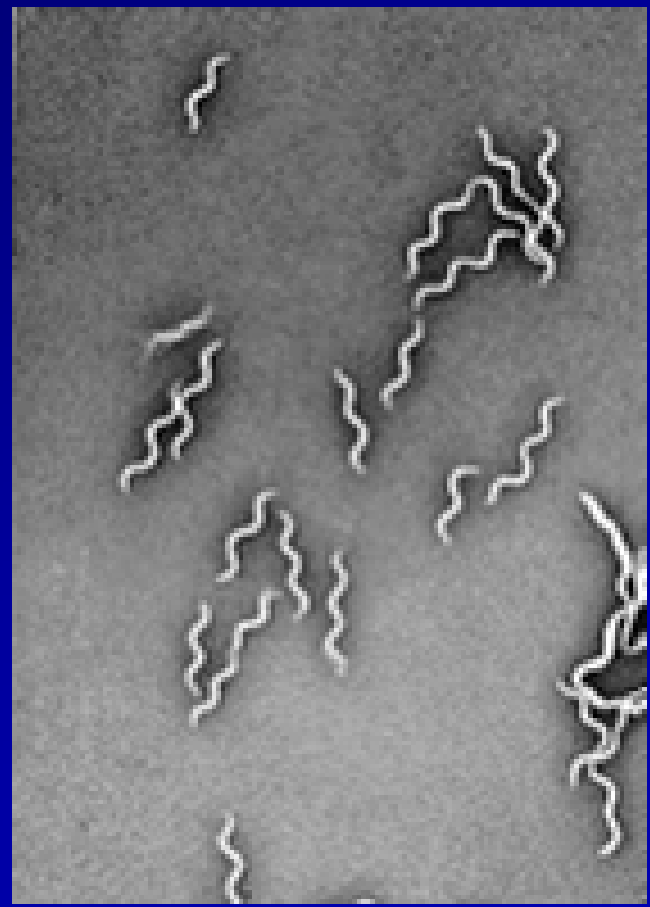
Krause, JAMA, 275:1657, 1996

Tick Born Relapsing Fever

- B. hermsii and B. turicatae in N. America
- Soft ticks (Ornithodoros), domestic animals
- Bite while sleeping; caves, crawling under house, cabins
- Ticks live near habitation
- Bite at night, feed less than 1 hour
- Live 15-20 years

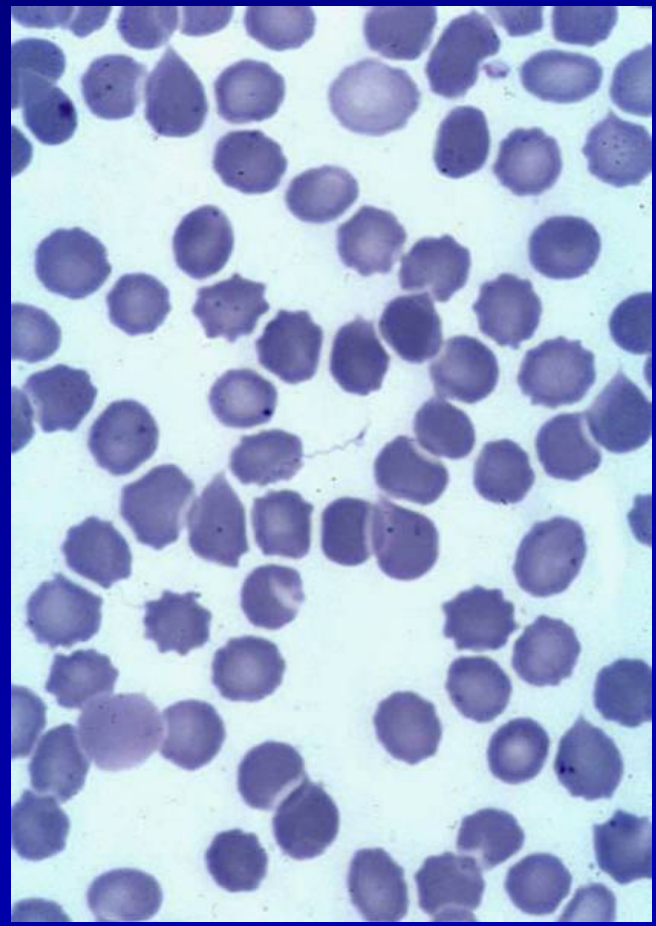
Tick Born Relapsing Fever

- Multiple febrile periods lasting 1-3 days
- Fever ends with “crisis” where most deaths occur (4-10%, <2% with RX)
- High fever, myalgia, neurological SX
- Leucopenia, anemia, thrombocytopenia
- EKG- QTc prolongation
- Hepatitis, CSF changes
- Fetal death, no malformations



Tick Born Relapsing Fever Diagnosis

- Thick smear, 0.5% acetic acid lysis (detects 104/ml)
- Thin smears (methanol fixed, 200 oil fields)
- Acridine orange or immunofluorescence
- Buffy coat, spun HCT (platelet layer)
- Wet mount (phase/DF, blood-PBS interface)
- Culture, PCR, ?serology



Dworkin, CID, 1998, 26:122

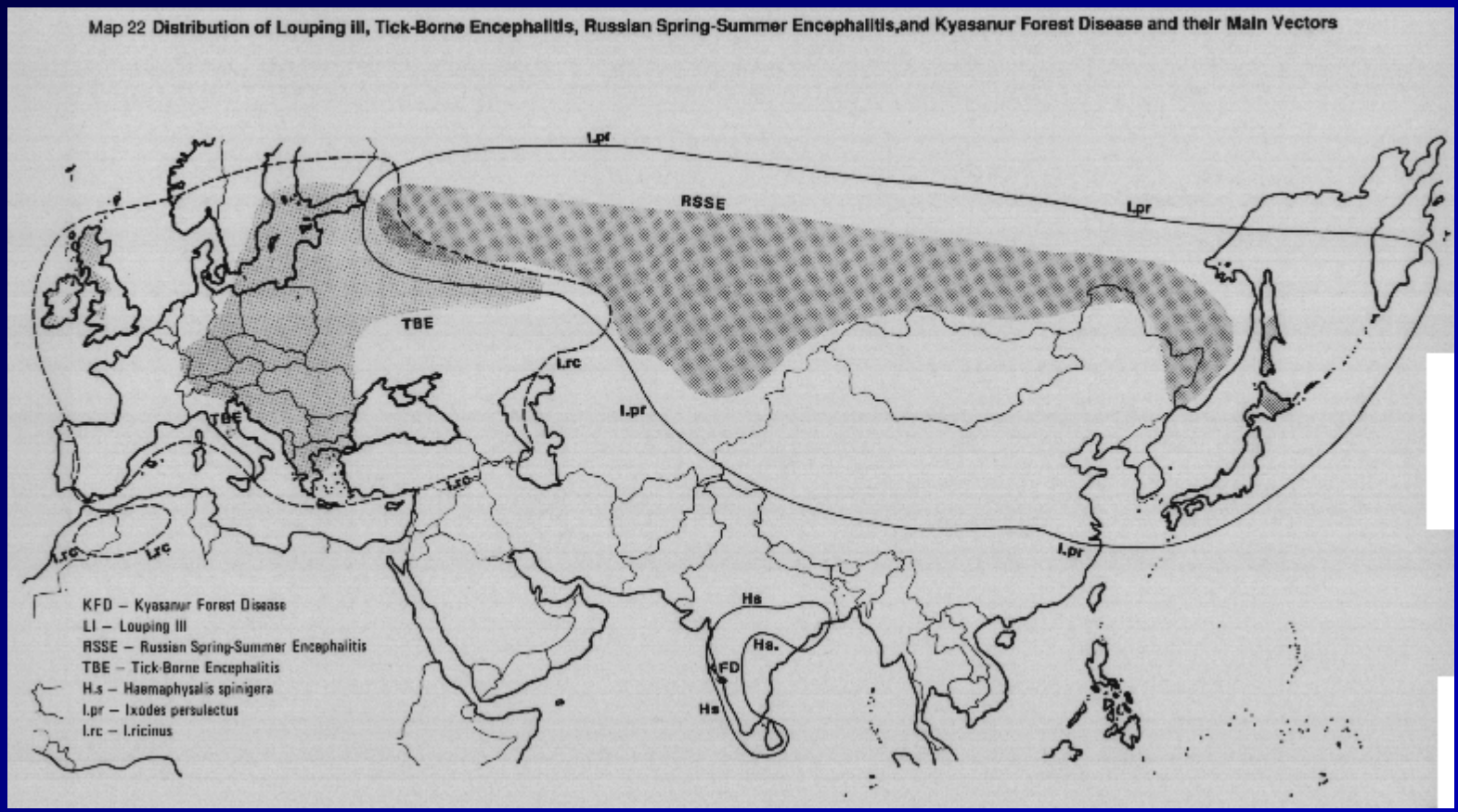
Tick Born Relapsing Fever Treatment

- RX- Doxycycline 100 mg bid x 10d,
- Alt erythromycin, penicillin
- Jarisch-Herxheimer reaction in 54% of PCN RX*
- 50% chance of infection after infected tick bite
  - Consider prophylactic TCN 500 mg qid x 2-3d within 2 d. of exposure

Tick Born Encephalitis

- RSSE- east Russia, China, Korea, Japan
- CEE-western USSR, Scandinavia, Europe
- Powassan- North America
- Elevation <1000 M, forest -field
- Peak JUN-JUL, OCT

Tick Born Encephalitis- Range

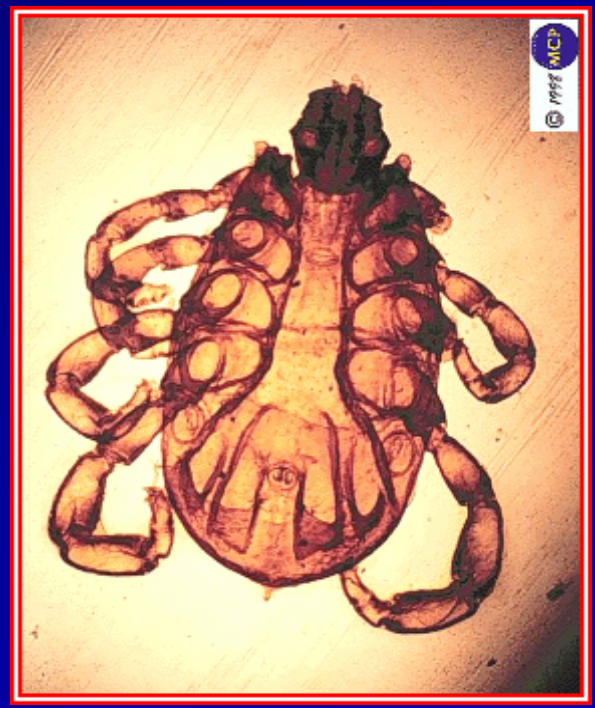


Tick Born Encephalitis

- Initial phase 1-8 d
- Asymptomatic days to 3 weeks
- 25% develop 2nd phase with meningitis, encephalitis, myelitis
- Symptoms 1 in 250 infected
- Only ½ of cases recall tick bite
- Some transmission through unpasteurized milk
- Few US soldiers seroconvert
- IND vaccine

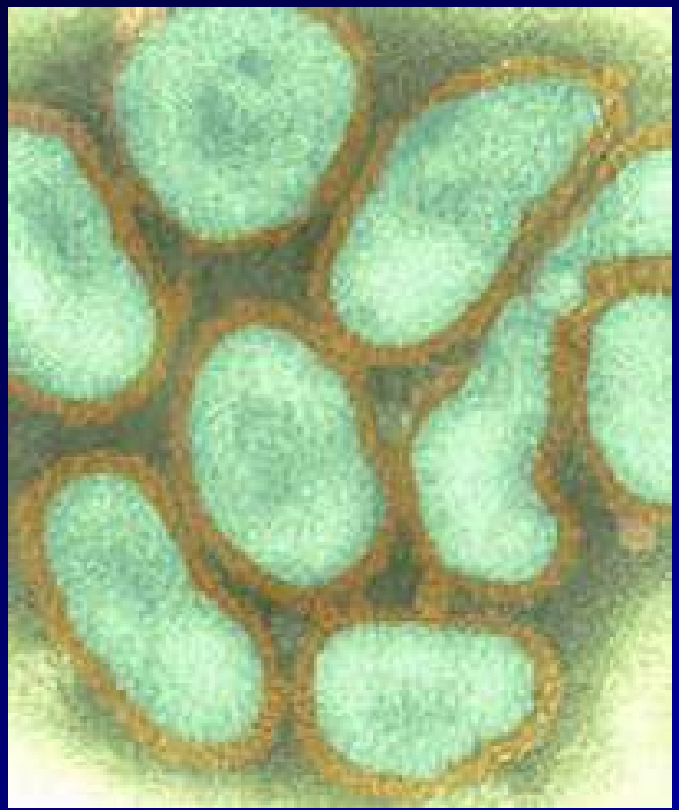
Congo-Crimean Hemorrhagic Fever

- Hyalomma ticks
- Immature- hares, hedgehogs, birds
- Mature- large wild and domestic animals
- USSR, Balkans, Middle east, Africa



Southern cattle tick

Congo-Crimean Hemorrhagic Fever



- Infects reticulo-endothelial cells, liver (hepatitis)
- Sudden fever, headache, limb pain, anorexia
- Vomiting, abdominal pain, diarrhea
- Flushing in face, chest
- Conjunctival injection
- Petechiae, enanthem, ecchymosis, bleeding
- 20-50% mortality
- Ribavirin
- Nosocomial transmission

Tick Paralysis

- Rare disease
- 6% mortality rate
- Children<10, girls>boys, spring, summer
- Salivary toxin action varied
  - Sodium channel
  - Acetylcholine release

Tick Paralysis

- Diplopia, dysarthria, dysphagia, drooling
- Isolated limb/facial paralysis
- Arm/leg ataxia may suggest cerebellar lesion
- Normal pupils, sensation
- Recovery within hours (Dermacenter)
  - 1-2d for I holocyclus